10726550a.trn

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626GMS

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 26	FEB 13	CASREACT coverage to be extended
NEWS 27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 30	Feb 26	MEDLINE reloaded with enhancements
NEWS 31	Feb 26	EMBASE enhanced with Clinical Trial Number field
NEWS 32	Feb 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 33	Feb 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 34	Feb 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT

MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:41:45 ON 10 MAR 2007

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:41:54 ON 10 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 MAR 2007 HIGHEST RN 925981-65-3
DICTIONARY FILE UPDATES: 9 MAR 2007 HIGHEST RN 925981-65-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

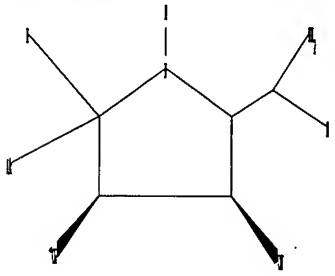
Please note that search-term pricing does apply when conducting SmartSELECT searches.

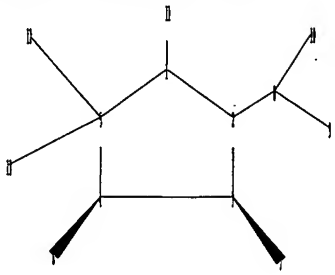
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

10726550a.trn

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10726550a.str





chain nodes :
6 7 8 9 10 11 12 13
ring nodes :
1 2 3 4 5
chain bonds :
1-11 2-8 3-7 4-6 5-12 5-13 8-9 8-10
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 3-7 4-6 5-13 8-10
exact bonds :
1-11 2-3 2-8 3-4 4-5 5-12 8-9
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS

Stereo Bonds:

6-4 (Single Wedge).
7-3 (Single Wedge).

Stereo Chiral Centers:

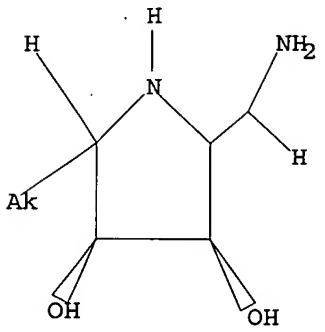
3 (Parity=Odd)
4 (Parity=Odd)

Stereo RSS Sets:

Type=Relative (Default). 2 Nodes= 3 4

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 14:42:09 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      108 TO ITERATE

100.0% PROCESSED      108 ITERATIONS                          1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         1537 TO     2783
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 14:42:16 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     2069 TO ITERATE

100.0% PROCESSED     2069 ITERATIONS                          9 ANSWERS
SEARCH TIME: 00.00.01

L3            9 SEA SSS FUL L1

=> FIL HCAPLUS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             172.10     172.31

FILE 'HCAPLUS' ENTERED AT 14:42:21 ON 10 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE COVERS 1907 - 10 Mar 2007 VOL 146 ISS 12
FILE LAST UPDATED: 9 Mar 2007 (20070309/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

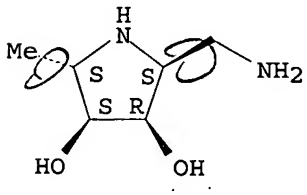
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 3 L3

=> d l4 ibib abs hitstr tot

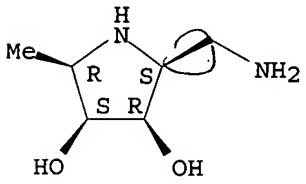
L4 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1060932 HCAPLUS
DOCUMENT NUMBER: 144:6996
TITLE: Stereoselective synthesis of (2S,3S,4R,5S)-5-methylpyrrolidine-3,4-diol derivatives that are highly selective α-L-fucosidase inhibitors
AUTHOR(S): Moreno-Vargas, Antonio J.; Carmona, Ana T.; Mora, Federico; Vogel, Pierre; Robina, Inmaculada
CORPORATE SOURCE: Department of Organic Chemistry, Faculty of Chemistry, University of Seville, Seville, E-41071, Spain
SOURCE: Chemical Communications (Cambridge, United Kingdom) (2005), (39), 4949-4951
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:6996
AB N-Phenylaminomethyl benzimidazolyl moieties attached at C-2 of (2S,3S,4R,5S)-5-methylpyrrolidine-3,4-diol increase the potency and selectivity of the inhibitory activity of these systems towards α-L-fucosidases.
IT 869857-93-2P 869857-94-3P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stereoselective synthesis of methylpyrrolidinediol derivs. as selective α-L-fucosidase inhibitors)
RN 869857-93-2 HCAPLUS
CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-methyl-, dihydrochloride, (2S,3R,4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 869857-94-3 HCAPLUS
CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-methyl-, dihydrochloride, (2S,3R,4S,5R)- (9CI) (CA INDEX NAME)

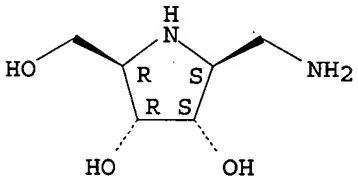
Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

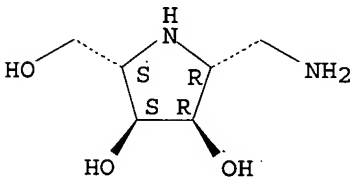
L4 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:400378 HCAPLUS
DOCUMENT NUMBER: 141:38786
TITLE: Syntheses and glycosidase inhibitory activities of 2-(aminomethyl)-5-(hydroxymethyl)pyrrolidine-3,4-diol derivatives
AUTHOR(S): Popowycz, Florence; Gerber-Lemaire, Sandrine; Schutz, Catherine; Vogel, Pierre
CORPORATE SOURCE: Institute of Chemical Sciences and Engineering, Swiss Federal Institute of Technology, EPFL-BCH, Lausanne, CH-1015, Switz.
SOURCE: Helvetica Chimica Acta (2004), 87(4), 800-810
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:38786
AB New 2-(aminomethyl)-5-(hydroxymethyl)pyrrolidine-3,4-diol derivs. were synthesized from (5S)-5-[(trityloxy)methyl]pyrrolidin-2-one and their inhibitory activities toward glycosidases were evaluated. The influence of the configuration of the pyrrolidine ring on glycosidase inhibition was evaluated. (2R,3R,4S,5R)-2-[(benzylamino)methyl]-5-(hydroxymethyl)pyrrolidine-3,4-diol was a good and selective inhibitor of α-mannosidase from jack bean (Ki = 1.2 μM) and from almond (Ki = 1.0 μM). Selectivity was lost for the non-benzylated derivative (2R,3R,4S,SR)-2-(aminomethyl)-5-(hydroxy-ethyl)pyrrolidine-3,4-diol which inhibited α-galactosidases, β-galactosidases, β-glucosidases, and α-N-acetylgalactosaminidase as well.
IT 704901-91-7P 704901-99-5P 704902-18-1P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(syntheses from (5S)-5-[(trityloxy)methyl]pyrrolidin-2-one and glycosidase inhibitory activities of 2-(aminomethyl)-5-(hydroxymethyl)pyrrolidine-3,4-diol derivs.)
RN 704901-91-7 HCAPLUS
CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-(hydroxymethyl)-, (2S,3S,4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



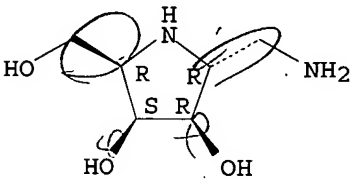
RN 704901-99-5 HCAPLUS
CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-(hydroxymethyl)-, (2R,3R,4S,5S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 704902-18-1 HCAPLUS
CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-(hydroxymethyl)-, (2R,3R,4S,5R)-(9CI) (CA INDEX NAME)

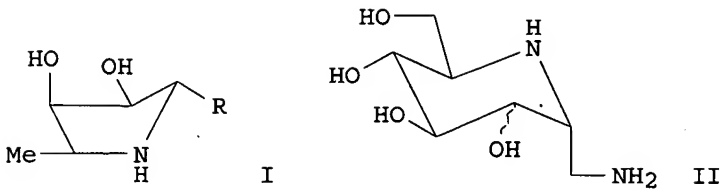
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

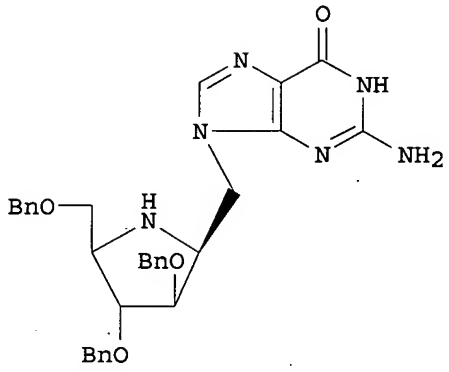
L4 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:433855 HCAPLUS
DOCUMENT NUMBER: 122:291430
TITLE: Synthesis and Evaluation of Homoaza Sugars as Glycosidase Inhibitors
AUTHOR(S): Wong, Chi-Huey; Provencher, Louis; Porco, John A., Jr.; Jung, Sang-Hun; Wang, Yi-Fong; Chen, Lihren; Wang, Ruo; Steensma, Darryl H.
CORPORATE SOURCE: Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of Organic Chemistry (1995), 60(6), 1492-501
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



I

II



III

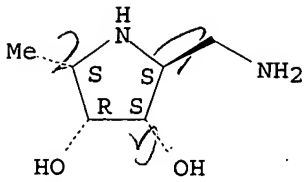
AB In an effort to develop transition-state mimetics of the glycosidase-catalyzed reaction, five- and six-membered azasugars and their homo-analogs were prepared and tested as inhibitors of glycosidases. Inhibition studies indicate that the fucosyl cation-like, five-membered imine and its reduced form I (R = H) are potent inhibitors of α-fucosidase from bovine kidney with resp. Ki values of 160 nM and 2 μM. The five-membered homoaminoaza sugar I (R = CH2NH2) is also a potent inhibitor of the enzyme (Ki = 1.9 + 10-6 M), while the glucose and mannose-like six-membered homoaminoaza sugars II are less potent than the corresponding 1-deoxyaza sugars as inhibitors of α-glucosidase and α-mannosidase, resp. The primary amino group was placed in an attempt to introduce addnl. electrostatic interactions in the active site. The inhibitory activities are, however, in the high μM range. Synthesis of homoaza sugars structurally related to a disaccharide and a nucleoside III is also described.

IT 162895-60-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of homoaza sugars as glycosidase inhibitors)

RN 162895-60-5 HCAPLUS

CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-methyl-, monohydrochloride, [2S-(2α,3β,4β,5β)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



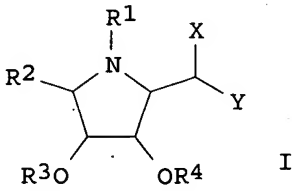

```
=> s azasugar
           133 AZASUGAR
           114 AZASUGARS
L5         199 AZASUGAR
                (AZASUGAR OR AZASUGARS)

=> s l5 and sugar chain enzyme
        258765 SUGAR
        130958 SUGARS
        330581 SUGAR
                  (SUGAR OR SUGARS)
        705584 CHAIN
        315788 CHAINS
        891260 CHAIN
                  (CHAIN OR CHAINS)
        801089 ENZYME
        464594 ENZYMES
       1015619 ENZYME
                  (ENZYME OR ENZYMES)
             3 SUGAR CHAIN ENZYME
                  (SUGAR(W)CHAIN(W)ENZYME)
L6           0 L5 AND SUGAR CHAIN ENZYME

=> s l5 and sugar chain
        258765 SUGAR
        130958 SUGARS
        330581 SUGAR
                  (SUGAR OR SUGARS)
        705584 CHAIN
        315788 CHAINS
        891260 CHAIN
                  (CHAIN OR CHAINS)
          3123 SUGAR CHAIN
                  (SUGAR(W)CHAIN)
L7           1 L5 AND SUGAR CHAIN

=> s l5 and sugar
        258765 SUGAR
        130958 SUGARS
        330581 SUGAR
                  (SUGAR OR SUGARS)
L8          70 L5 AND SUGAR

=> s l5 and configuration
```

```
        293529 CONFIGURATION
         87370 CONFIGURATIONS
        353806 CONFIGURATION
                 (CONFIGURATION OR CONFIGURATIONS)
L9           19 L5 AND CONFIGURATION

=> s l9 and py<=2001
      21882175 PY<=2001
L10          11 L9 AND PY<=2001

=> s l10 and enzyme
        801089 ENZYME
        464594 ENZYMES
       1015619 ENZYME
                 (ENZYME OR ENZYMES)
L11           4 L10 AND ENZYME

=> d his

     (FILE 'HOME' ENTERED AT 14:41:45 ON 10 MAR 2007)

     FILE 'REGISTRY' ENTERED AT 14:41:54 ON 10 MAR 2007
L1               STRUCTURE UPLOADED
L2             1 S L1
L3             9 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 14:42:21 ON 10 MAR 2007
L4             3 S L3
L5           199 S AZASUGAR
L6             0 S L5 AND SUGAR CHAIN ENZYME
L7             1 S L5 AND SUGAR CHAIN
L8            70 S L5 AND SUGAR
L9            19 S L5 AND CONFIGURATION
L10           11 S L9 AND PY<=2001
L11            4 S L10 AND ENZYME

=> d l7 ibib abs hitstr tot

L7   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2003:76749  HCAPLUS
DOCUMENT NUMBER:          138:137514
TITLE:                    Preparation of azasugar compounds as
                          specific inhibitors against sugar
                          chain related enzymes
INVENTOR(S):              Kanie, Osamu; Saotome, Chikako
PATENT ASSIGNEE(S):       Mitsubishi Chemical Corporation, Japan
SOURCE:                   PCT Int. Appl., 57 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2003008379         A1    20030130    WO 2002-JP5672           20020607
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
```

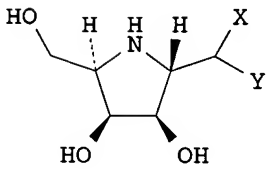
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004147591 A1 20040729 US 2003-726550 20031204
PRIORITY APPLN. INFO.: JP 2001-173855 A 20010608
WO 2002-JP5672 A2 20020607
OTHER SOURCE(S): MARPAT 138:137514

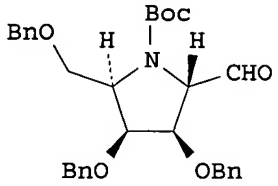
GI



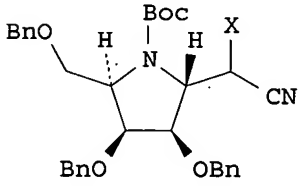
I



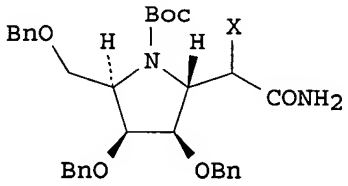
II



III



IV



V

AB Compds. represented by the general formula (I) or salts thereof [wherein R1 is hydrogen, optionally substituted C1-10 alkyl, or an N-protecting group; R2 is optionally substituted C1-10 alkyl or optionally substituted C2-10 alkenyl; R3 and R4 are each independently hydrogen or a hydroxyl-protecting group; X is -N(R5)R6 or a residue derived from the amino group of an amino acid or a peptide (wherein R5 and R6 are each independently hydrogen, optionally substituted C1-10 alkyl, or optionally substituted C3-12 cycloalkyl); and Y is hydrogen, CH2NH2, CONH2, or CO2H] are prepared These compds. are useful as specific inhibitors against sugar chain related enzymes including glycosyltransferase and glycosidase, and effective in the treatment or prevention of diseases in which sugar chain related enzymes participate. They also inhibit α-GalNAc-ase (2-acetamido-2-deoxy-α-D-galactoside acetamidodeoxygalactohydrolase, an inactivation factor of macrophage activation factor) and thereby are useful as antiviral agents, anticancer agents, and immunostimulants. A small library of 27 iminocyclitols [II; X = BuNH, Me2NCH2CH2NH, Me(CH2)9NH, HOCH2CH2NH, 1-adamantylamino, MeO(CH2)3NH, tetrahydrofuran-2-ylmethylamino, phenethylamino, cyclohexylamino; Y = H, CH2NH2, CONH2] were prepared by (1) reductive amination of an aldehyde (III)

with various amines (e.g. phenethylamine) followed by deprotection and (2) Strecker reaction of the aldehyde with trimethylsilyl cyanide with various amines and Pd-catalyzed hydrogenolysis of the resulting amino nitriles (IV; X = same as above) or conversion of the amino nitriles IV into amino carboxamides (V; X = same as above) followed by Pd-catalyzed hydrogenolysis. The compds. II showed a broad spectrum of inhibitory activity against enzymes tested including α-glucosidase, α-mannosidase, α-galactosidase, β-galactosidase, and α-GalNAc-ase, α-1,3-galactotransferase, and β-1,4-galactotransferase, but none of the compds. showed α-glucosidase-inhibitory activity comparable to that of deoxynojirimycin. The structure-activity relationship for the enzyme inhibitory activity was also discussed.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l10 ibib abs hitstr tot

L10 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:30733 HCAPLUS

DOCUMENT NUMBER: 136:212683

TITLE: α-Retaining glucosyl transfer catalysed by trehalose phosphorylase from Schizophyllum commune: mechanistic evidence obtained from steady-state kinetic studies with substrate analogues and inhibitors

AUTHOR(S): Nidetzky, Bernd; Eis, Christian

CORPORATE SOURCE: Institute of Food Technology, University of Agricultural Sciences Vienna (BOKU), Vienna, A-1190, Austria

SOURCE: Biochemical Journal (2001), 360(3), 727-736
CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fungal trehalose phosphorylase is classified as a family 4 glucosyltransferase that catalyzes the reversible phosphorolysis of α,α-trehalose with net retention of anomeric configuration. Glucosyl transfer to and from phosphate takes place by the partly rate-limiting interconversion of ternary enzyme-substrate complexes formed from binary enzyme-phosphate and enzyme-α-D-glucopyranosyl phosphate adducts resp. To advance a model of the chemical mechanism of trehalose phosphorylase, we performed a steady-state kinetic study with the purified enzyme from the basidiomycete fungus Schizophyllum commune by using alternative substrates, inhibitors and combinations thereof in pairs as specific probes of substrate-binding recognition and transition-state structure. Orthovanadate is a competitive inhibitor against phosphate and α-D-glucopyranosyl phosphate, and binds 3 x 104-fold tighter (K1 1 μM) than phosphate. Structural alterations of D-glucose at C-2 and O-5 are tolerated by the enzyme at subsite + 1. They lead to parallel effects of approx. the same magnitude (slope = 1.14; r2 = 0.98) on the reciprocal catalytic efficiency for reverse glucosyl transfer [log (Km/kcat)] and the apparent affinity of orthovanadate determined in the presence of the resp. glucosyl acceptor (log Ki). An adduct of orthovanadate and the nucleophile/leaving group bound at subsite +1 is therefore the true inhibitor and displays partial transition state analogy. Isofagomine binds to subsite -1 in the enzyme-phosphate complex with a dissociation constant of 56 μM and inhibits trehalose phosphorylase at least 20-fold better than 1-deoxynojirimycin.

The specificity of the reversible azasugars inhibitors would be explained if a pos. charge developed on C-1 rather than O-5 in the proposed glucosyl cation-like transition state of the reaction. The results are discussed in the context of α-retaining glucosyltransferase mechanisms that occur with and without a β-glucosyl enzyme intermediate.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:845492 HCAPLUS
DOCUMENT NUMBER: 136:114658
TITLE: Biochemical and structural assessment of the 1-N-azasugar GalNAc-isofagomine as a potent family 20 β-N-acetylhexosaminidase inhibitor
AUTHOR(S): Mark, Brian L.; Vocadlo, David J.; Zhao, Dalian; Knapp, Spencer; Withers, Stephen G.; James, Michael N. G.
CORPORATE SOURCE: Department of Biochemistry, Canadian Institutes of Health Research Group in Protein Structure and Function, University of Alberta, Edmonton, AB, T6G 2H7, Can.
SOURCE: Journal of Biological Chemistry (2001), 276(45), 42131-42137
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

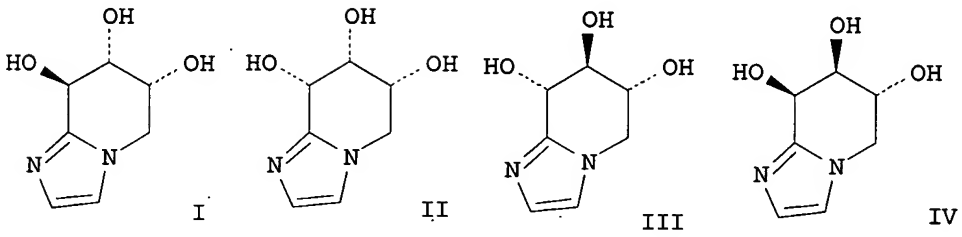
AB Azasugar inhibitors of the isofagomine class are potent competitive inhibitors of configuration-retaining β-glycosidases. This potency results from the formation of a strong electrostatic interaction between a protonated endocyclic nitrogen at the anomeric center of the inhibitor and the catalytic nucleophile of the enzyme. Although the majority of retaining β-glycosidases use a mechanism involving a carboxylate residue as a nucleophile, Streptomyces plicatus β-N-acetylhexosaminidase (SpHEX) and related family 20 glycosidases lack such a catalytic residue and use instead the carbonyl oxygen of the 2-acetamido group of the substrate as a nucleophile to attack the anomeric center. Thus, a strong electrostatic interaction between the inhibitor and enzyme is not expected to occur; nonetheless, the 1-N-azasugar (2R,3R,4S,5R)-2-acetamido-3,4-dihydroxy-5-hydroxy methyl-piperidinium hydrochloride (GalNAc-isofagomine·HCl), which was synthesized and assayed for its ability to inhibit SpHEX, was found to be a potent competitive inhibitor of the enzyme (Ki = 2.7 μM). A crystallog. complex of GalNAc-isofagomine bound to SpHEX was solved and refined to 1.75 Å and revealed that the lack of a strong electrostatic interaction between the anomeric center of GalNAc-isofagomine and SpHEX is compensated for by a novel 2.8-Å hydrogen bond formed between the equatorial proton of the endocyclic nitrogen of the azasugar ring and the carboxylate of the general acid-base residue Glu-314 of SpHEX. This interaction appears to contribute to the unexpected potency of GalNAc-isofagomine toward SpHEX.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:830177 HCAPLUS
DOCUMENT NUMBER: 136:200356
TITLE: Carbohydrate transition state mimics, I Synthesis of

	imidazolo-piperidinopentoses as nagstatine analogues
AUTHOR(S):	Gessier, Francois; Tschamber, Theophile; Tarnus, Celine; Neuburger, Markus; Huber, Walter; Streith, Jacques
CORPORATE SOURCE:	Ecole Nationale Superieure de Chimie, Universite de Haute-Alsace, Mulhouse, 68093, Fr.
SOURCE:	European Journal of Organic Chemistry (2001), (21), 4111-4125 CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER:	Wiley-VCH Verlag GmbH
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 136:200356

GI



AB The syntheses of the four imidazolo-piperidino-pentoses (I-IV), which belong to the D-series, and of their L-enantiomers, are reported. Ascorbic acid and isoascorbic acid were converted over several steps into the L-threo/L-erythro- and the D-erythro/D-threo-configured aldotetroses, resp., which are the key building blocks for the eight target imidazolo-pentoses cited above. Nucleophilic addition of a metalated imidazole to any one of these four aldotetroses gave the corresponding two diastereomeric adducts, intramol. cyclisation of which provided the expected bicyclic target mols., with some protection and deprotection steps being unavoidable prerequisites. The structures and configurations of all eight I-IV were determined unambiguously, by a combination of 1H/13C NMR spectroscopy, CD (CD) and [α]D values, in conjunction with single-crystal X-ray diffraction analyses of the L-arabino and D-lyxo aza-sugars ent-3 and 6. Although lacking the hydroxymethylene group in the C(5) position, the overall structure of these eight stereomers strongly resembles that of the natural product nagstatine, a potent inhibitor of N-acetyl-β-D-glucosaminidase. As a matter of fact, after examination of the inhibitory properties of these imidazolo-piperidinoses against six commonly encountered glycosidases, we observe that the L-arabino imidazolo-sugar ent-I is a potent inhibitor in this series, with Ki = 1 μM both with a β-glucosidase and with a β-galactosidase. The D-ribo and D-xylo stereomers II and III proved to be inhibitors of a β-glucosidase of similar magnitude (II: Ki = 20 μM; III: Ki = 17 μM), the other stereomers being either modest to poor inhibitors, or showing no inhibition at all.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2001:145753 HCAPLUS
DOCUMENT NUMBER:	134:193654
TITLE:	Stereoselective synthesis of arabinose-derived phosphonates. [Erratum to document cited in

CA128:167630]
AUTHOR(S): Bouix, Claire; Bisseret, Philippe; Eustache, Jacques
CORPORATE SOURCE: Laboratoire de Synthese Organique et Chimie Microbienne Associe, Ecole Nationale Superieure de Chimie de Mulhouse Associe au CNRS, Universite de Haute-Alsace, Mulhouse, F-68093, Fr.
SOURCE: Tetrahedron Letters (2000), 41(17), 3269
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The phosphonate 1 and its cyclic precursors (Scheme 1) all have the 2(R) configuration (instead of 2(S) as originally proposed). Accordingly, the carbamate 8 has the 2(S) configuration. The phosphonate 3 has the 2(S) configuration (instead of 2(R) as originally proposed).

L10 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:756196 HCAPLUS
DOCUMENT NUMBER: 134:71806
TITLE: A general approach to the synthesis of dideoxy and trideoxyiminoalditols from β-D-glycosides
AUTHOR(S): Pistia, G.; Hollingsworth, R. I.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Michigan State University, East Lansing, MI, 48824, USA
SOURCE: Carbohydrate Research (2000), 328(4), 467-472
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:71806
AB Imino sugars (also called azasugars), a class of compds. of which the 1,5-dideoxy and 1,5,6-trideoxyiminoalditols are members, are important glycosidase inhibitors with very high potential as drugs. Their potential therapeutic applications range from the treatment of diabetes to cancer and AIDS. We present here a general method for the preparation of such compds. with the D-gluco and D-galacto configurations starting from β-D-glycosides. The procedure is especially appealing because of its high stereoselectivity and straightforwardness. The key steps are the selective oxidation of the glycosides to hexulosonic acids and reduction of the oxime derivs. to lactams, which are further reduced to the target compds. The C-6 position can be deoxygenated during the reduction if it bears an acetoxy group. Trideoxy imino sugars are then produced. Deacetylation prior to oxime reduction gives dideoxy compds.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:498609 HCAPLUS
DOCUMENT NUMBER: 133:252629
TITLE: A norbornyl route to azasugars: a new synthesis of deoxynojirimycin analogues
AUTHOR(S): Mehta, G.; Mohal, N.
CORPORATE SOURCE: Department of Organic Chemistry, Indian Institute of Science, Bangalore, 560 012, India
SOURCE: Tetrahedron Letters (2000), 41(30), 5741-5745
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:252629
AB A new synthesis of deoxynojirimycin (DNJ) analogs (galacto- and altro-configuration) has been achieved through a functionalized cyclopentene derivative crafted from the norbornyl system, employing double reductive amination as the key step. The new DNJ analogs have been evaluated against various glycosidases and found to be moderate to strong inhibitors.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:327708 HCAPLUS
TITLE: General approach to the synthesis of imino-dideoxy and -trideoxy alditols from glycosides.
AUTHOR(S): Pistia, Gabriela; Hollingsworth, Rawle I.
CORPORATE SOURCE: Department of Chemistry, Michigan State University, East Lansing, MI, 48824, USA
SOURCE: Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), CARB-032. American Chemical Society: Washington, D. C.
CODEN: 69CLAC
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Imino-sugars (also called azasugars) a class of compds. of which the 1,5-diimino-1,5-dideoxy and 1,5-diimino-1,5,6-trideoxy alditols are members, are important glycosidase inhibitors with very high potential as drugs. Their potential therapeutic applications range from the treatment of diabetes to cancer and AIDS. We present here a general method for the preparation of such compds. with the D-gluco and D-galacto configurations starting from glycosides. The procedure is especially appealing because of its high stereoselectivity and straighforwardness.

L10 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:91214 HCAPLUS
TITLE: Control of the anomeric configuration of bicyclic azasugars by remote substitution
AUTHOR(S): Fan, Jianmei; Berges, David A.; Zhang, Na; Gonda, Shaun; Mower, Kendall
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, 84602, USA
SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), CARB-054. American Chemical Society: Washington, D. C.
CODEN: 67GHA6
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Most azasugars reported so far consist of either one ring or two rings which share a nitrogen atom and lack a heteroatom comparable to the glycosidic oxygen atom present in sugars. It is well known that glycosidases are exquisitely selective regarding the anomeric configuration of their substrates, and it appears that the selectivity of inhibition of glycosidases by azasugars with a glycosidic heteroatom can also be related to their anomeric configuration. As an approach to enhancing inhibitory selectivity, we have sought ways to control the anomeric configuration of azasugars which have an anomeric

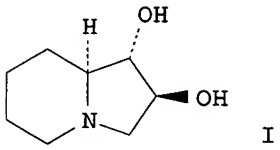
heteroatom. Almost exclusive formation of a single anomeric product occurs when Me substituents are added to that ring of bicyclic azasugars which itself does not mimic a sugar. The synthesis and characterization of several examples will be described.

L10 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:39347 HCAPLUS
DOCUMENT NUMBER: 128:128209
TITLE: Conformation of 5-amino-5-deoxypentonolactams
AUTHOR(S): Kefurt, Karel; Havlicek, Jaroslav; Hamernikova, Michaela; Kerfurtova, Acenka; Votavova, Hana
CORPORATE SOURCE: Department Chemistry Natural Compounds, Prague Institute Chemical Technology, Prague, 166 28, Czech Rep.
SOURCE: Collection of Czechoslovak Chemical Communications (1997), 62(12), 1919-1930
CODEN: CCCCAK; ISSN: 0010-0765
PUBLISHER: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Four configuration isomers of 5-amino-5-deoxy-D-pentonolactam and their tri-O-acetyl derivs. were studied using NMR and CD spectroscopy. For all compds. chemical shifts of the 1H and 13C nuclei as well as of vicinal coupling consts. were obtained. Comparison of the observed 3J(H,H) with those calculated for various conformations by a modified Karplus relationship led to the assignment of predominant conformation 3H4(D) or 4H3(D) to the lactams in solution The most important factor for determining the conformation seems to be the pseudo-equatorial position of the substituent on the carbon next to the carbonyl group. The results of the CD spectra of the lactams in water, interpreted according to the currently used rules, agreed with the NMR results.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:727837 HCAPLUS
DOCUMENT NUMBER: 127:346586
TITLE: N-thiocarbonyl azasugars: a new family of carbohydrate mimics with controlled anomeric configuration
AUTHOR(S): Blanco, Jose L. Jimenez; Diaz Prez, Victor M.; Mellet, Carmen Ortiz; Fuentes, J.; Garcia Fernandez, Jose M.; Diaz Arribas, Juan C.; Canada, Francisco J.
CORPORATE SOURCE: Departamento de Quimica Organica, Facultad de Quimica, Universidad de Sevilla, Seville, E-41071, Spain
SOURCE: Chemical Communications (Cambridge) (1997), (20), 1969-1970
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bicyclic azasugar glycomimetics structurally related to the polyhydroxy-indolizine and -piperidine series incorporating a stereoelectronically controlled pseudoanomeric axial hydroxy group have been prepared by tautomeric rearrangement of cyclic thiocarbamate precursors; preliminary enzyme inhibition tests show an increased selectivity towards yeast α-glucosidase for the α-D-glucopyranose analog as compared with castanospermine or nojirimicin.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:833624 HCAPLUS
DOCUMENT NUMBER: 123:314224
TITLE: Assignment of the Absolute Configuration of Natural Lentiginosine by Synthesis and Enzymic Assays of Optically Pure (+) and (-)-Enantiomers
AUTHOR(S): Brandi, Alberto; Cicchi, Stefano; Cordero, Franca M.; Frignoli, Roberta; Goti, Andrea; Picasso, Sylviane; Vogel, Pierre
CORPORATE SOURCE: Dipartimento di Chimica Organica U. Schiff, Centro di studio C. N. R. sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, Florence, I-50121, Italy
SOURCE: Journal of Organic Chemistry (1995), 60(21), 6806-12
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:314224
GI



I

AB The structure and absolute configuration of natural (+)-lentiginosine (I) isolated from plant sources was determined to be (1S,2S,8aS)-1,2-dihydroxyindolizidine on the basis of synthesis of both enantiomers and their inhibition of amyloglucosidases. (+)-I was derived from (L)-(+)-tartaric acid via a highly stereo- and regioselective 1,3-dipolar cycloaddn. of (3S,4S)-3,4-bis[(tert-butyldiphenylsilyl)oxy]-1-pyrroline N-oxide to methylenecyclopropane, followed by thermal rearrangement of the adduct into (1S,2S,8aS)-1,2-[(tert-butyldiphenylsilyl)oxy]octahydroindolizin-7-one. (-)-I was derived in the same way from (D)-(-)-tartaric acid. Both (+)-I and (-)-I displayed inhibition specificity for amyloglucosidases, being inactive toward 17 other glycosidases. With amyloglucosidase from Aspergillus niger, (+)-I displayed inhibition (Ki = 2 μM) 5 times stronger than that reported for natural lentiginosine, 35 times that measured for (-)-I, and twice that of castanospermine. (+)-I is thus the most potent and specific competitive inhibitor of amyloglucosidases among azasugars and their analogs.

=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:30733 HCAPLUS
DOCUMENT NUMBER: 136:212683
TITLE: α-Retaining glucosyl transfer catalysed by trehalose phosphorylase from Schizophyllum commune:

mechanistic evidence obtained from steady-state kinetic studies with substrate analogues and inhibitors

AUTHOR(S): Nidetzky, Bernd; Eis, Christian

CORPORATE SOURCE: Institute of Food Technology, University of Agricultural Sciences Vienna (BOKU), Vienna, A-1190, Austria

SOURCE: Biochemical Journal (2001), 360(3), 727-736
CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fungal trehalose phosphorylase is classified as a family 4 glucosyltransferase that catalyzes the reversible phosphorolysis of α,α-trehalose with net retention of anomeric configuration. Glucosyl transfer to and from phosphate takes place by the partly rate-limiting interconversion of ternary enzyme-substrate complexes formed from binary enzyme -phosphate and enzyme-α-D-glucopyranosyl phosphate adducts resp. To advance a model of the chemical mechanism of trehalose phosphorylase, we performed a steady-state kinetic study with the purified enzyme from the basidiomycete fungus Schizophyllum commune by using alternative substrates, inhibitors and combinations thereof in pairs as specific probes of substrate-binding recognition and transition-state structure. Orthovanadate is a competitive inhibitor against phosphate and α-D-glucopyranosyl phosphate, and binds 3 x 104-fold tighter (K1 1 μM) than phosphate. Structural alterations of D-glucose at C-2 and O-5 are tolerated by the enzyme at subsite + 1. They lead to parallel effects of approx. the same magnitude (slope = 1.14; r2 = 0.98) on the reciprocal catalytic efficiency for reverse glucosyl transfer [log (Km/kcat)] and the apparent affinity of orthovanadate determined in the presence of the resp. glucosyl acceptor (log Ki). An adduct of orthovanadate and the nucleophile/leaving group bound at subsite +1 is therefore the true inhibitor and displays partial transition state analogy. Isofagomine binds to subsite -1 in the enzyme -phosphate complex with a dissociation constant of 56 μM and inhibits trehalose phosphorylase at least 20-fold better than 1-deoxynojirimycin. The specificity of the reversible azasugars inhibitors would be explained if a pos. charge developed on C-1 rather than O-5 in the proposed glucosyl cation-like transition state of the reaction. The results are discussed in the context of α-retaining glucosyltransferase mechanisms that occur with and without a β-glucosyl enzyme intermediate.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:845492 HCAPLUS

DOCUMENT NUMBER: 136:114658

TITLE: Biochemical and structural assessment of the 1-N-azasugar GalNAc-isofagomine as a potent family 20 β-N-acetylhexosaminidase inhibitor

AUTHOR(S): Mark, Brian L.; Vocadlo, David J.; Zhao, Dalian; Knapp, Spencer; Withers, Stephen G.; James, Michael N. G.

CORPORATE SOURCE: Department of Biochemistry, Canadian Institutes of Health Research Group in Protein Structure and Function, University of Alberta, Edmonton, AB, T6G 2H7, Can.

SOURCE: Journal of Biological Chemistry (2001),

276(45), 42131-42137
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Azasugar inhibitors of the isofagomine class are potent competitive inhibitors of configuration-retaining β-glycosidases. This potency results from the formation of a strong electrostatic interaction between a protonated endocyclic nitrogen at the anomeric center of the inhibitor and the catalytic nucleophile of the enzyme. Although the majority of retaining β-glycosidases use a mechanism involving a carboxylate residue as a nucleophile, Streptomyces plicatus β-N-acetylhexosaminidase (SpHEX) and related family 20 glycosidases lack such a catalytic residue and use instead the carbonyl oxygen of the 2-acetamido group of the substrate as a nucleophile to attack the anomeric center. Thus, a strong electrostatic interaction between the inhibitor and enzyme is not expected to occur; nonetheless, the 1-N-azasugar (2R,3R,4S,5R)-2-acetamido-3,4-dihydroxy-5-hydroxy methyl-piperidinium hydrochloride (GalNAc-isofagomine·HCl), which was synthesized and assayed for its ability to inhibit SpHEX, was found to be a potent competitive inhibitor of the enzyme (Ki = 2.7 μM). A crystallog. complex of GalNAc-isofagomine bound to SpHEX was solved and refined to 1.75 Å and revealed that the lack of a strong electrostatic interaction between the anomeric center of GalNAc-isofagomine and SpHEX is compensated for by a novel 2.8-Å hydrogen bond formed between the equatorial proton of the endocyclic nitrogen of the azasugar ring and the carboxylate of the general acid-base residue Glu-314 of SpHEX. This interaction appears to contribute to the unexpected potency of GalNAc-isofagomine toward SpHEX.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

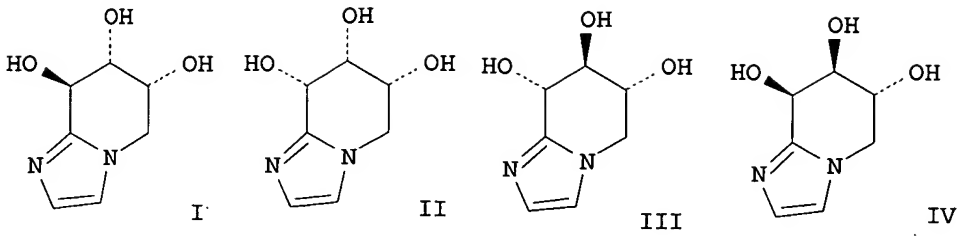
ACCESSION NUMBER: 2001:830177 HCAPLUS
DOCUMENT NUMBER: 136:200356

TITLE: Carbohydrate transition state mimics, I Synthesis of imidazolo-piperidinopentoses as nagstatine analogues

AUTHOR(S): Gessier, Francois; Tschamber, Theophile; Tarnus, Celine; Neuburger, Markus; Huber, Walter; Streith, Jacques
CORPORATE SOURCE: Ecole Nationale Superieure de Chimie, Universite de Haute-Alsace, Mulhouse, 68093, Fr.

SOURCE: European Journal of Organic Chemistry (2001), (21), 4111-4125
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:200356

GI



I II III IV

AB The syntheses of the four imidazolo-piperidino-pentoses (I-IV), which belong to the D-series, and of their L-enantiomers, are reported. Ascorbic acid and isoascorbic acid were converted over several steps into the L-threo/L-erythro- and the D-erythro/D-threo-configured aldotetroses, resp., which are the key building blocks for the eight target imidazolo-pentoses cited above. Nucleophilic addition of a metalated imidazole to any one of these four aldotetroses gave the corresponding two diastereomeric adducts, intramol. cyclisation of which provided the expected bicyclic target mols., with some protection and deprotection steps being unavoidable prerequisites. The structures and configurations of all eight I-IV were determined unambiguously, by a combination of 1H/13C NMR spectroscopy, CD (CD) and [α]D values, in conjunction with single-crystal X-ray diffraction analyses of the L-arabino and D-lyxo aza-sugars ent-3 and 6. Although lacking the hydroxymethylene group in the C(5) position, the overall structure of these eight stereomers strongly resembles that of the natural product nagstatine, a potent inhibitor of N-acetyl-β-D-glucosaminidase. As a matter of fact, after examination of the inhibitory properties of these imidazolo-piperidinoses against six commonly encountered glycosidases, we observe that the L-arabino imidazolo-sugar ent-I is a potent inhibitor in this series, with Ki = 1 μM both with a β-glucosidase and with a β-galactosidase. The D-ribo and D-xylo stereomers II and III proved to be inhibitors of a β-glucosidase of similar magnitude (II: Ki = 20 μM; III: Ki = 17 μM), the other stereomers being either modest to poor inhibitors, or showing no inhibition at all.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:727837 HCAPLUS
DOCUMENT NUMBER: 127:346586
TITLE: N-thiocarbonyl azasugars: a new family of carbohydrate mimics with controlled anomeric configuration
AUTHOR(S): Blanco, Jose L. Jimenez; Diaz Prez, Victor M.; Mellet, Carmen Ortiz; Fuentes, J.; Garcia Fernandez, Jose M.; Diaz Arribas, Juan C.; Canada, Francisco J.
CORPORATE SOURCE: Departamento de Quimica Organica, Facultad de Quimica, Universidad de Sevilla, Seville, E-41071, Spain
SOURCE: Chemical Communications (Cambridge) (1997), (20), 1969-1970
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bicyclic azasugar glycomimetics structurally related to the polyhydroxy-indolizine and -piperidine series incorporating a stereoelectronically controlled pseudoanomeric axial hydroxy group have

been prepared by tautomeric rearrangement of cyclic thiocarbamate precursors; preliminary enzyme inhibition tests show an increased selectivity towards yeast α-glucosidase for the α-D-glucopyranose analog as compared with castanospermine or nojirimicin.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	100.09	272.40

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-14.82	-14.82

STN INTERNATIONAL LOGOFF AT 14:51:07 ON 10 MAR 2007